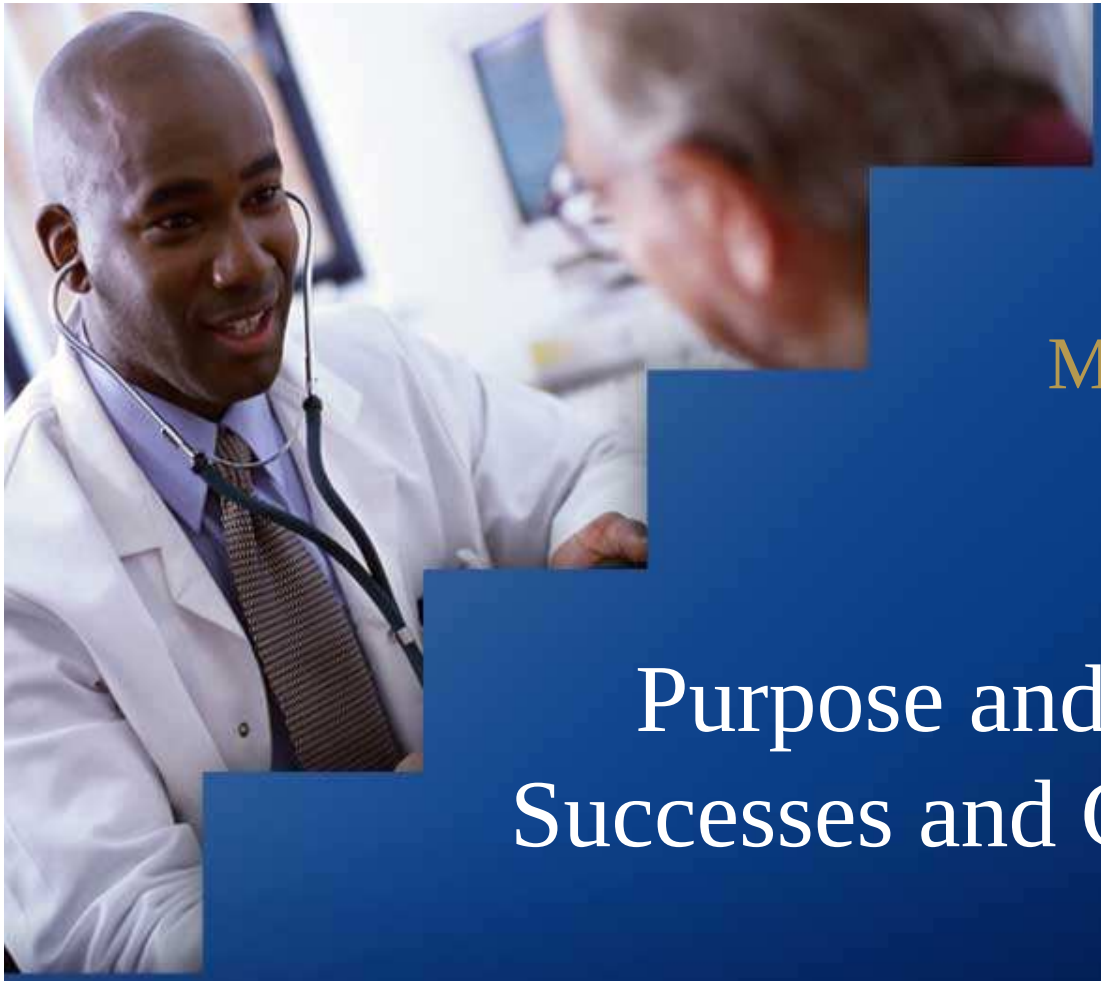

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Purpose and Function of IRBs: Successes and Current Challenges

AAHRPP®
Association for the Accreditation of Human Research Protection Programs, Inc.®

Very brief history

- United States became enlightened about research abuses in the 1960's and 1970's
- National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - Ethical principles for conducting research
  - Oversight of research

History of IRBs

- 1953 NIH required independent review and participants' written consent at least for research involving patient volunteers or "unusual hazard"
- 1954 NIH extended the requirements to all intramural research involving normal volunteers
- 1966 NIH required independent review of research by a committee of the investigator's "institutional associates" for extramural research (did not apply to intramural research at NIH). Separate policy for intramural research
- 1974 review committees codified in regulations

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National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

- Produced many reports – best known is the Belmont Report
  - Three ethical principles that govern the conduct of research
  - Report on institutional review boards
    - Argument for local review boards
    - Oversight and educational purpose

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Ethical principles for conducting research

- Respect for persons
  - Autonomous individuals
  - Diminished autonomy
- Beneficence
  - Do no harm
  - Maximize benefits
- Justice
  - Burdens and benefits should be shared

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Oversight of research

- Institutional review boards
  - "at least five members with varying backgrounds to promote complete and adequate review of research of research activities commonly conducted by the institution" sit on the IRB.
  - The role of the IRB is indirectly defined in the regulations: The IRB should be constituted in such a way as to promote the respect for its advice and counsel in safeguarding the rights and welfare of research participants.

What is respect?

- The IRB derives legitimacy within the institution by being sufficiently qualified through the experience and expertise of its members and legitimacy in the community through its diversity—including consideration of race, gender, and cultural background—and sensitivity to community attitudes.

Composition of the IRB

- No IRB may consist of all men or all women.
- IRBs must have at least one member whose primary concerns are in scientific areas.
- IRBs must have at least one member whose primary concerns are in nonscientific areas.
- IRBs must have at least one member who is not otherwise affiliated with the institution (this requirement extends to immediate family members).
- No IRB member with a conflicting interest may participate in the initial or continuing review of a proposed study, except to provide information requested by the remaining IRB members.

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Responsibilities of IRBs

Requirements in regulations

- Initial review and approval of research
- Primary reviewer systems
- Expedited procedures for review
- Consent
- Notification of investigators
- Continuing review
- Minutes
- Records retention

Requirements by OHRP

- Research determinations
- Exemption determinations
- Relevant materials for review
- Documentation of determinations and protocol-specific findings

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Federal requirements of institutions that are often imposed on IRBs to carry out

- Assurance of compliance
- IRB roster
- Procedures the IRB will follow for conducting initial and continuing review of research and reporting its findings to the investigator and the institution
- Procedures for determining which projects require review more frequently than annually
- Procedures for prompt reporting of unanticipated problems involving risk to subjects or others
- Procedures for prompt reporting of serious or continuing non-compliance
- Procedures for prompt reporting of suspensions and terminations
- Procedures for verification by a third party of no material changes since the last IRB review

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IRBs

- Primary function: determine that research is ethically justifiable
  - Risks are minimize
  - Risks are reasonable in relation to any anticipated benefits to participants and the importance of the knowledge that is reasonable expected to result
  - Selection of participants is equitable
  - Consent will be sought and documented
  - Research plan makes adequate provisions for monitoring the data to ensure safety
  - Adequate provisions to protect the privacy of participants and maintain confidentiality of data

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Government scrutiny of IRBs

- 1996 — General Accounting Office - heavy workloads, lack of preparedness of IRB, limited resources
- 1998 — Office of Inspector General, DHHS - IRBs overwhelmed; issued a warning signal
- 1998 — Suspensions of research programs at major academic centers
- 2000 — OHRP determination letters posted on the Web
- FDA inspections and warning letters

FDA warning letters to IRBs

52 warning letters were issued to IRBs from Jan 1997 to July 2004

VIOLATION THEME	Number of IRBs (%) with this violation
Inadequate written procedures	50 (96%)
Inadequate documentation of IRB activities	47 (90%)
Inadequate continuing review	36 (69%)
Inappropriate membership/quorum requirements	30 (58%)
Inappropriate consent process	19 (37%)
Inadequate initial review	11 (21%)

Ref: Bramstedt, A and Kassimatis, K. Clin Invest Med 27:6 (Dec 2004): 316-323

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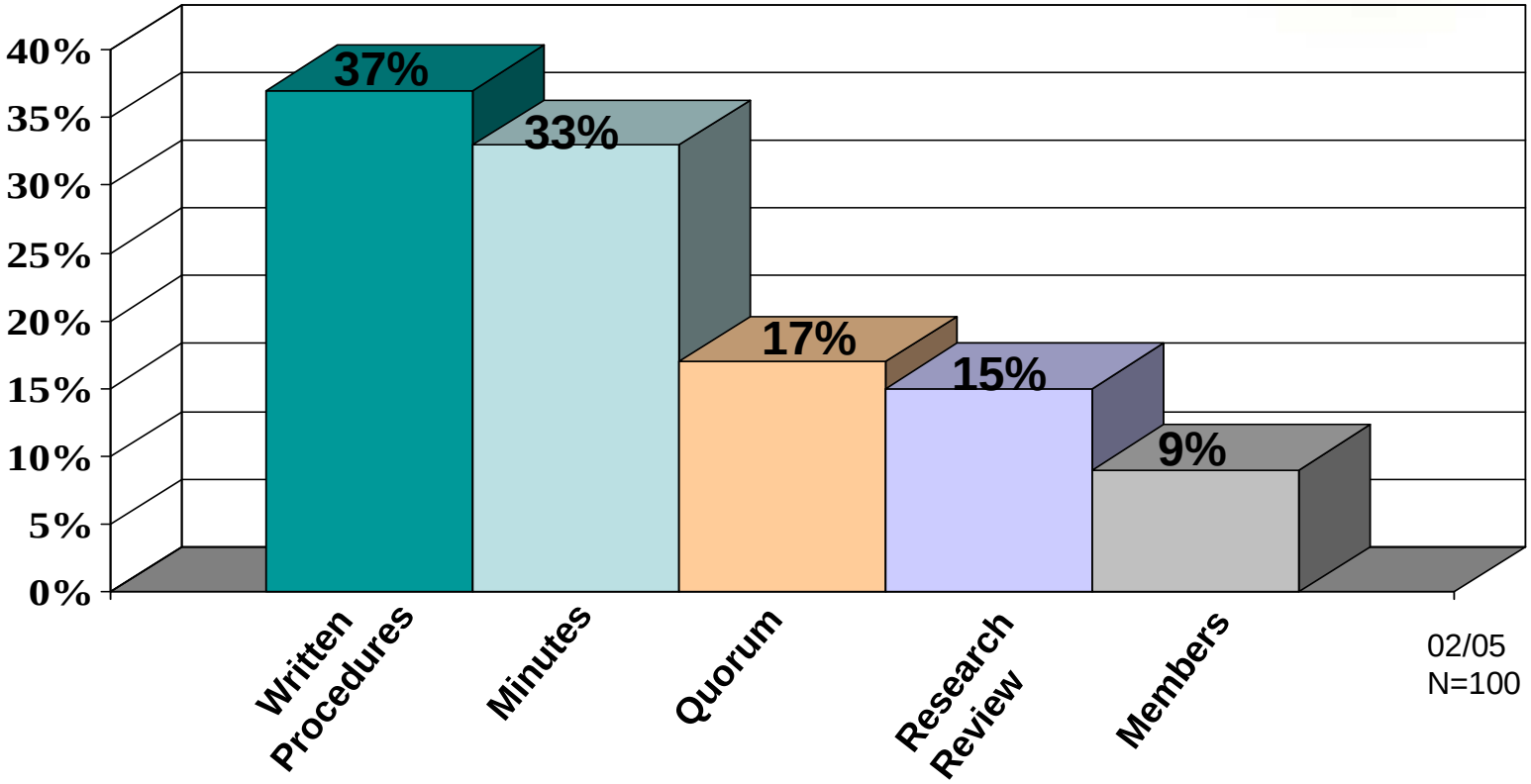
IRB inspections by FDA

What deficiencies were most common in FY'04?



Ref: J. Rhoads, DSI Update to SQA Regulatory Forum, 12 May 2005

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Reactions by the research community

- More resources for IRBs
- Those whose research programs were suspended infused more than $1,000,000 into their IRBs
- Sugarman et al found that the annual operating costs ranges from $171,014 to $4,705,333, with a median cost of $741,920.
- Higher visibility of the IRB function
- Risk averse behavior on part of institution and IRB

Virtually no research on the effectiveness of IRBs

- Are protections better than prior to 1974?
  - No data are available to answer this question
  - Studies like that the Tuskegee Syphilis Study do not exist today
  - Most probably agree that protections are better today than 30 years ago
  - Regulatory compliance is better than 30 years ago

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From the perspective of accreditation

- IRBs miss some of the criteria for approving research
  - IRB do not make the assessment that risks are reasonable in relation to the importance of the knowledge that can reasonably be expected to occur
  - Privacy interests are confused with confidentiality of data
  - Provisions for data monitoring to ensure safety are not understood
  - Additional protections for vulnerable populations are not understood

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From the perspective of accreditation

- IRB chairs and staff are more knowledgeable and IRB staff are more expert in the regulations
- Institutions have much better policies and procedures
- Continuing review procedures are better
- Expedited review procedures are better
- Ownership of responsibility for protecting research participants is broader

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Challenges for IRBs

- Perception of IRB seems to be as negative
- Researchers believe there is more burden
- Review of multi-site studies
- Rise in popularity of regional IRBs
- Competitive priorities within institutions
- Clear guidance from OHRP and FDA

Should we keep our current IRB system?

- No Congressional legislation is likely to pass
- Strong pressure for status quo
- Need more education for IRBs and researchers
- Alternative models of IRBs should be tested
- IRBs need to take on a business model, including cost recuperation, continuous quality improvement, and promotion of services

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